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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/835,922	04/16/2001	Fang Liang Zhang	CN01167K	9049

24265 7590 12/17/2002

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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No.	Applicant(s)	
	09/835,922	ZHANG ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *4-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This office action is response to Applicant's election of Group I, drawn to claims 1-3. Election was made with traverse in Paper No. 9 (10/16/02). The traversal is on the ground(s) that Inventions I, II and III are classified into two different subclasses only and the Office has not provided any reason or showing that serious burden will result by examining all the groups. This argument is not persuasive. The Office has provided the reasons for separating the three groups in Paper No. 8 (09/13/02). For example, Inventions I and III are independent and distinct, each from the other, because the methods are practiced with materially different process steps for materially different purposes and each method requires a non-coextensive search because of the different modes of operation, process steps and goals. Specifically, the different methods require different ingredients, process steps and endpoints. Inventions of group I are directed to identifying an agonist and antagonist of a mammalian SP168 receptor, while Invention III is directed to treatment methods. A serious burden will be placed on the Office, when searching for methods identifying agonist and antagonist and method of treating a medical condition caused by SP168. For example, searching for treatment methods will not necessarily generate the agonist and antagonist of the receptor. Similarly, searching for agonist and antagonist will not result in treatment methods. Finally, invention II is drawn to pharmaceutical composition that can be used in materially different processes, such as diagnostic assays or antibody production. Therefore, the restriction requirement is deemed proper and made FINAL. Claims 1-3 are pending.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: A method for identifying an agonist or antagonist of a mammalian SP168 receptor.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The instant claims are directed to a method for identifying an agonist or antagonist of a mammalian SP168 receptor. It is alleged that SP168 protein belongs to G protein-coupled receptor family (GPCR). These claims are drawn to an invention with no apparent or disclosed patentable utility. The applicant claims that the SP168 receptor is expressed almost exclusively in human brain and spinal tissue (Page 2, lines 1-5). They claim that the expression was especially prevalent in substania nigra, hippocampus, putamen, amygdala, thalamus, paraventricular, arcuate and interpeduncular nuclei. It is asserted that such an expression pattern points to the possible role of the SP168 receptor in neurodegenerative disorders such as Parkinson's, Alzheimer's, Huntington's, Amyotrophic lateral sclerosis (ALS) and Multiple sclerosis (MS). Thus, they assert that the identification of the ligands for the SP168 receptor

will provide critical tools necessary to evaluate the precise role of the SP168 receptor in such medical conditions (Page 2, lines 7-9). It is further asserted that identification of the ligands for SP168 receptor is an important first step in the development of agonists and antagonists of the receptor (Page 2, lines 9-11). Novel biological molecules lack well-established utility and must undergo extensive experimentation.

The applicant states that the SP168 receptor sequence is 1187 nucleotides (SEQ ID NO: 1) long with an ORF encoding 342 amino acid (SEQ ID NO: 2) residues (Page 3, lines 31-35). They claim that the endogenous ligand of the SP168 receptor that was purified from rat spinal cord by chromatography was identified as being ADP by Mass spectroscopy (Page 4, lines 15-17). It is asserted that the pharmacology of SP168 was characteristic of P2Y receptor, a class of G-protein coupled receptors activated primarily by ATP, ADP, UTP and UDP (Page 4, lines 23-25). Applicant's claim that the instant protein belongs to a G protein-coupled receptor family is presumably because of sequence homology between the instant invention (SP168 protein sequence) and various known G protein-coupled receptors. However, Ji et al. (J. Biol. Chem. 273 (28): 17299-17302) indicate that G protein coupled receptors are classified into over 100 subfamilies according to sequence homology, ligand structure and receptor function. A substantial degree of amino acid homology is found among members of a particular subfamily, but comparison between subfamilies show significantly less or no similarity. Mutant G-protein coupled receptors are incapable of binding ligand or generating normal signals, constitutively generate signals, or are not appropriately expressed on the cell surface (Page 17299, paragraphs 1 and 2). Also, "an increasing number of G protein-coupled receptor subfamilies show diverse modes of ligand binding, signal generation, transmembrane signal

transduction, and signal transfer to various cytoplasmic signal molecules other than G-protein" (Page 17302, paragraph 4). Furthermore, since the specification does not disclose any methods or working examples that demonstrate the polynucleotide and polypeptide of the instant application exhibit similar activities of other G protein-coupled receptors, the skilled artisan would not be able to categorize the polynucleotide and polypeptide of the instant application as a G protein-coupled receptor. Additionally, the specification of the instant application does not teach the skilled artisans which domains of human SP168 protein sequence are structurally related to other G protein-coupled receptors. One skilled in the art would not know the utility and function of human SP168 protein, even if it was a putative G protein coupled receptor because, as discussed in the related art above and the specification of the instant application, neither the prior art nor the specification provides for the physiological significance of the claimed receptor. Neither the specification nor the prior art demonstrates a causal correlation or nexus of the claimed polypeptide with any of the conditions or disorders contemplated by the instant specification, therefore, there is no evidence of record that would provide for method of identifying an agonist or antagonists of a mammalian SP168 receptor. There is absolutely no evidence of record or any line of reasoning that would support a conclusion that the "SP168" receptor protein of the instant application is involved in any of the neurodegenerative disorders.

There is little doubt that, after complete characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and, until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that of which was addressed in *Brenner v. Manson*,

148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which required that an invention must have either an immediate obvious or fully disclosed "real-world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility," "[u]nless and until a process is refined and developed to this point - where specific benefit exists in currently available form - there is insufficient justification for permitting an applicant to engross what may prove to be a broad field," and "a patent is not a hunting license," "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a method of identifying an agonist or antagonist of a mammalian SP168 receptor. Applicant has disclosed the cDNA sequence (SEQ ID NO: 1) and amino acid (SEQ ID NO: 2) of SP168. Applicant also claims that the SP168 receptor was shown to be express in the human CNS tissue and spinal cord by dot blot (page 23, lines 20-21). However, there is no actual and specific significance that can be attributed to said polypeptides and the polynucleotides identified in the specification or the art of record, except the prophetic recitation of potential uses, which include the use of this SP168 receptor protein and the nucleotides in identifying an agonist or antagonist. For this reason, the instant invention is incomplete. Since, neither the prior art nor the specification provides for the physiological significance of the disclosed and claimed receptor or its ligand, there is no immediately obvious patentable use for it. In

addition, the instant specification does not disclose a "real-world" use for said polypeptides and polynucleotides, except the prophetic recitation of potential uses, which include possible use in identifying agonist or antagonists of SP168. Also, there are no working examples that demonstrate any specific utility.

Furthermore, post filing publication of Hollopeter et al. (2001), describes the identification of the platelet ADP receptor ($P2Y_{12}$), a G-protein coupled receptor protein which is expressed to a lesser extent in the brain and abundantly in the platelets (Page 204, figure 4). This protein has 100% sequence identity to (SEQ ID No: 2) of the instant invention (See Appendix A). Unlike the instant invention that claims that the SP168 receptor is involved in the neurodegenerative disorders, $P2Y_{12}$ is involved in the thrombotic disorders based on mutational analysis and pharmacological studies. Thus, the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4a. Claims 1-3 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above (Paragraph 4), one skilled in the art clearly would not know how to use the claimed invention to identify

the agonist or antagonists of SP168 receptor. Furthermore, even if utility was established it will not be enabled for reasons set forth above.

4b. Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses SP168 receptor having amino acid sequence SEQ ID No: 2 (Page 3, lines 29-34). These disclosures meet the written description and enablement provisions of 35 USC 112, first paragraph. However, the specification does not disclose any other fragments of SEQ ID NO: 2. The claims as written, however, encompass various amino acid sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 1 and 2. The specification does not provide written support for the genus encompassed by the instant claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*See Vas-Cath* at page 1116).

With the exception of isolated amino acid sequence of SEQ ID No: 2, the skilled artisan cannot envision all the detailed chemical structures of the claimed amino acid sequences, regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only an isolated amino acid sequence of SEQ ID No: 2 but not the full breadth of the claims encompassing the various fragments meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. As a result, it does not appear that the inventors were in possession of the various amino acid sequences set forth in claims 1 and 2. Claim 2 is rejected insofar as it depends on 1.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5a. Claims 1-2 are rejected as being vague and indefinite in the recitation of the term "G protein coupled receptor SP168". The protein of interest is described by an arbitrary protein name. It is unclear from which vertebrate species the nucleic acid encoding the said protein was isolated. Applicant should particularly point out and distinctly claim the SP168 by claiming structural characteristics associated with the protein (e.g. amino acid sequence, molecular weight, etc.). Claiming biochemical molecules by a particular

name given to the protein by various workers in the field fails to distinctly claim what that protein is. Applicant is required to provide SEQ ID Nos to isolated nucleic acid and protein sequences.

5b. Claim 1 is rejected as vague and indefinite for reciting the term "fragment thereof", because the specification does not clearly define the term "fragment thereof".

6. No Claims are allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph. D whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and 703-308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JS
December 14, 2002

JEFFREY STUCKER
PRIMARY EXAMINER